

REMARKS/ARGUMENTS

Claim 20 is amended for better format and further incorporation of the limitations of previously presented claims 25 and 26. Claims 28 and 29 are amended for better format. Claim 26 is amended to recite that the diluent has a pH of 2.0-3.0, which can find support at page 15, lines 5-7 of the originally filed specification. Claims 35-38 are newly added. Support for new claims 35-37 can be found at page 16, lines 12-14 of the originally filed specification. Support for new claim 38 can be found at originally filed claims, pages 3-20 of the originally filed specification. No new matter is added. Entry of the above amendments is respectfully requested. Upon entry of the above amendments, claims 20-21, 24, 26, 28-31, and 35-38 are pending. Reconsideration of the present application in view of the above amendments and the following remarks is respectfully solicited.

The previously presented claims 20-21 and 24-31 are all rejected under 35 U.S.C. §112, first paragraph, as not enabled by the specification. According to the Examiner, an urine sample may comprise solid components such as erythrocytes, leukocytes, epithelial cells, urinary casts, bacteria, fungi, crystals, and mucus threads. The Examiner states that although the specification provides guidance on how to discriminate bacteria from components, such as contaminants (mucus, crystals, amorphous salts and cell fragments), it is unclear how to discriminate bacteria from other components such as erythrocytes and reticulocytes that are also components of the urine that have high affinity for the dyes. Applicants respectfully traverse.

First, even if there were some inoperative embodiments within the claimed scope of the present application, it would not necessarily follow that the claims of the present application are not enabled under 35 U.S.C. §112, first paragraph. As instructed by MPEP2164.08(b),

The presence of inoperative embodiments within the scope of a claim does not necessarily render a claim nonenabled. The standard is whether a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with expenditure of no more effort than is normally required in the art. *Atlas*

Powder Co. v. E.I. du Pont de Nemours & Co., 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984) (prophetic examples do not make the disclosure nonenabling).

Nor are Applicants aware of any relevant law, rules, or guidance, that requires a claimed invention to be operable under any conceivable condition. Here, independent claim 20 is directed to a method of preparing an assay sample for detecting bacteria in a urine sample by a flow cytometer. Independent claim 38 is directed to method of staining bacteria. Under the pertinent rules set forth above, these claims are enabled, as long as the specification provide some guidance teaching how the assay sample prepared in claim 20 or the staining method recited in claim 38 is used under normal circumstances. Applicants are not required to demonstrate that the method of claim 20 or 38 is applicable to any urine sample, such as a urine sample which contains erythrocytes and leukocytes in an amount so substantial that the presence of erythrocytes and leukocytes will affect the bacteria detection. Indeed, as disclosed by Inoue J (U.S. Patent No. 5,891,733), which is cited by the Examiner, "For example, the measurement of erythrocytes is important in determining whether there is bleeding in the passageway from the nephric glomerulus to urethra. Appearance of leukocytes suggests suspicion about renal disease such as pyelonephritis, leading to early discovery of inflammation and infectious disease." This indicates that a urine sample does not normally comprise erythrocytes and leukocytes, much less reticulocytes, which are young erythrocytes immediately after a release of denucleated erythroblastic cells in bone marrow into peripheral blood (see column 1, lines 15-17 of Akai et al (U.S. Patent No. 5,891,731)) cited by the Examiner, in a substantial amount.

Second, contrary to the Examiner's statement, sufficient guidance has been provided in the specification of the present application regarding "how to use" the present invention. For example, at page 7, line s 5-10, the originally filed specification discloses: "the cationic surfactant may be suitably used since the cationic surfactant not only improves the stainability of bacteria but also dissolves/shrinks mucous fibers, erythrocytes, cell fractures and others which are present in a sample and thereby reduces their effect on detection of bacteria." At page 15, lines 1-6, the originally filed specification discloses: " Where a urine

sample is stained at an acidic pH, (1) bacteria is stained better than in a neutral or alkaline state and (2) nonspecific staining of mucus threads is prevented and the mucus threads is lysed to a certain extent. Thus, the acidic state is advantageous to the bacteria staining.” Acidic pH and cationic surfactant are now all recited in independent claims 20 and 38.

In addition, at page 2, line 24 to page 3, line 2, the originally filed specification discloses, “USP 4,622,298, and Japanese Unexamined Patent Publication No. Hei 9 (1997)-119926 and No. Hei 9 (1997)-329596 each proposes a method of detecting bacteria in a fluorescence-stained urine sample with a flow cytometer.” For example, U.S. Patent No. 4,622,298, which is cited in the originally filed specification of the present application, discloses a method for the assessment of bacteriuria and pyuria, which includes the simultaneous detection and quantitation of microorganisms, leukocytes and squamous epithelial cells in a urine specimen. The three cell types are stained with a fluorescent dye, and the urine specimen is analyzed directly, preferably by a single flow microfluorometry protocol. U.S. Patent No. No. 4,622,298 discloses in detail in the specification, in particular Examples 1-4, regarding to how to detect bacteria, ieukocytes, and squamous epithelial cells in a urine sample by a single flow cytometer. Note that, “Since every patent is presumed valid (35 U.S.C. § 282), and since that presumption includes the presumption of operability (*Metropolitan Eng. Co. v. Coe*, 78 F.2d 199, 25 USPQ 216 (D.C.Cir. 1935), examiners should not express any opinion on the operability of a patent.” See MPEP 716.07.

Like U.S. Patent No. No. 4,622,298 and other references discussed in the background section of the specification of the present application, the present invention also relates to detecting bacteria in a fluorescence-stained urine sample with a flow cytometer. Moreover, the present invention allows quicker and more efficient detection of bacteria than the prior art method even if a sample contains nitrite ions at high concentration. Therefore, the claims of the present application are sufficiently enabled in view of the specification and other patents and publications dated prior to the filing date of the present application,

such as those references discussed in the background section of the specification of the present application.

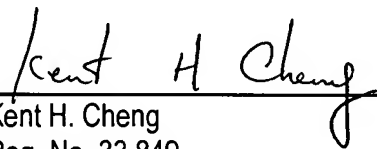
Third, Applicants have now replaced the term "discriminate" previously recited in claim 1 with "detect" to clarify that the assay sample obtained in accordance with claim 1 is used to detect the presence of bacteria in a urine sample, not to discriminate bacteria from every other ingredient that may potentially exist in the urine sample in any amount. As to new claim 38, it also does not recite the term "discriminate."

For at least the above reasons, sufficient guidance has been provided in the specification so that a person of ordinary skill in the art would be able to know how to make and how to use the invention described in the pending claims of present application. The claims are, therefore, in compliance with the enablement requirement set forth under 35 U.S.C. §112, first paragraph. Applicants respectfully request that the Examiner withdraw the rejections under 35 U.S.C. §112, first paragraph.

Based on the foregoing, Applicants believe that the present application is now in condition of allowance. Early and favorable consideration is earnestly requested.

if any additional fees or charges are required at this time, they may be charged to our Patent and Trademark Office Deposit Account No. 03-2412.

Respectfully submitted,
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